REMARKS

Status of the Claims

Claims 1-9, 13, 14, and 17-23 are currently pending. In the instant Response, claims 1, 5, 9, 13, 14, and 19 are amended; and new claims 24-45 are added. Thus, after entry of these amendments, claims 1-9, 13, 14, and 17-45 are presented for consideration.

Pursuant to the Office Action, claims 1-9, 13, 14, and 17-23 are rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out an distinctly claim the subject matter which Applicants regard as the invention. Claims 1-3, 5-9, and 17-23 are rejected under 35 U.S.C. §112, first paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the Claim Amendments

Support for the claim amendments can be found throughout the specification, in general. Amendments to claims 13 and 14 drawn to a polynucleotide having 95% and 97% identity, respectively, to SEQ ID NO:4 and encoding a polypeptide having alpha galactosidase activity can be found, *inter alia,* at page 9, lines 10-12. Other amendments to claims 1, 5, 9, 13, 14, and 19 merely clarify the scope of the claims and do not change the scope of the claims. Support for new claims 24-28 directed to polynucleotides that hybridize to polynucleotides that encode for a polypeptide having alpha galactosidase activity can be found, *inter alia,* at page 5, lines 1-10; page 5, line 22, to page 6, line 10; and page 7, line 25, to page 8, line 8. Support for new claims 29-30 directed to fragments encoding a polypeptide having alpha galactosidase activity can be found, *inter alia,* at page 7, line 24, to page 8, line 8; and page 10, lines 7-11 and 14-25. Support for new claims 31-41 to fragments can be found, *inter alia*, at page 8, line 14-25; and page 9, lines 17- 23. Support for new claims 42-45 wherein the fragments form part of a probe can be

found, *inter alia*, at page 8, line 14, to page 9, line 6. Accordingly, no new matter has been introduced by the instant amendments.

Specification Informalities

The Patent Office alleges that the title of the invention is not descriptive. Applicants submit that the invention is directed to the discovery of a novel polypeptide having alpha galactosidase activity. While the source of the alpha galactosidase is *Thermococcus alcaliphilus,* the claims are not limited to alpha galactosidases from *Thermococcus alcaliphilus*. Accordingly, Applicants submit that the suggested title "*Thermococcus alcaliphilus* Alpha galactosidase" is not accurate. Applicants have changed the title to, "Alpha-galactosidase Enzymes, Nucleic Acids Encoding Them and Methods for Making and Using Them." Applicants submit that the objection to the title has been overcome with the instant amendment.

Issues under 35 U.S.C. §112, second paragraph

Claims 1-9, 13, 14, and 17-23 are rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Patent Office alleges that claim 1 and claim 5 are indefinite in the recitation of "a polynucleotide that is complementary." It alleges that neither the specification nor the claims provides a definition of the term "complementary" and that it is unclear whether the complementary strand is a partial or complete complement.[1] Applicants respectfully submit that one of ordinary skill in the art would understand that "complementary" would mean that a nucleic acid strand is "complementary" to another nucleic acid strand when the bases of one strand is capable of forming bonds with the base of the other strand, *e.g.,* the classic pairing being A:T/U and C:G. Thus, one choosing to construct a complementary strand to a "first polynucleotide" could design the complementary strand to be completely complementary to the "first polynucleotide." However, one skilled in the art would also recognize that there could be a

[1] See page 2, lines 21-24, of the Office Action.

naturally occurring complementary strand of the "first polynucleotide" that also contains mismatched base pairings and is, therefore, not completely complementary. Thus, the skilled artisan would recognize that the complementary strand does not need to be completely complementary. Accordingly, Applicants respectfully submit that one of ordinary skill in the art would recognize the scope of the clamed invention.

The Patent Office alleges that claim 9 is unclear in the recitation of "process of producing a cell," as it finds that it is unclear how the recited steps results in the production of a cell.[2] Applicants have amended claim 9 to recite "a process of producing a cell that expresses a polynucleotide encoded by a DNA contained in a vector comprising providing a cell and transforming or transfecting the cell with a vector of claim 6." This amendment clarifies that the type of cell being produced is one that can express the polypeptide of the invention and that it can be made by transforming or transfecting the cell with a vector containing DNA. Applicants respectfully submit that the instant amendment merely clarifies the scope of claim 9 and does not change the scope of the claim.

The Patent Office alleges that claim 13 (and dependent claims 14 and 19) is unclear for the recitation of "protein having enzymatic activity."[3] Applicants have amended claim 13 to recite to a protein having alpha galactosidase activity. The instant amendment was made to clarify the scope of claim 13 (which depends from and incorporates all the limitations thereof) and does not change the scope of the claim.

Applicants respectfully submit that the amendments and reasons provided herein overcome all the rejections based upon 35 U.S.C. §112, second paragraph, raised by the Patent Office. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection as applied to claims 1, 5, 9, and 13, as well as all the claims that depend therefrom, *i.e.*, claims 2-4, 6-8, 14, and 17-23.

---

[2] See page 3, lines 3-4, of the Office Action.
[3] See page 3, lines 6-7, of the Office Action.

Issues under 35 U.S.C. §112, first paragraph

Written Description

Claims 1-3, 5-9, and 17-23 are rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art hat the inventors, at the time the application was filed had possession of the claimed invention.

The Patent Office alleges that claims 1 and 5 (as well as claims depending therefrom) are directed to a genus of polynucleotides as set forth in claim 1a, claim 1c, claim 5a, and claim 5c. The Patent Office alleges that the specification does not contain any disclosure of the function of all polynucleotides comprising homologues or fragments of a polynucleotide encoding SEQ ID NO:4. Therefore, the Patent Office alleges that many functionally unrelated polynucleotides are encompassed within the scope of the claims.[4] Applicants respectfully disagree. Applicants have amended claims 1 and 5 to more particularly describe the claimed nucleotides and have added new claims 29 and 31, and claims that depend therefrom, to clarify the issues.

Amended claims 1 and 5 are directed to an isolated polynucleotide having at least 70% or 90% identity, respectively, to a polynucleotide encoding a polypeptide as set forth in SEQ ID NO:4. The claimed polynucleotide must further encode a polypeptide having alpha galactosidase activity. In other words, the polynucleotides of the claimed invention encode polypeptides having alpha galactosidase activity. Thus, the polynucleotides of the claimed invention would not encompass functionally unrelated polynucleotides as alleged by the Patent Office.[5] The claimed polynucleotides are described in terms of their structure and function. Accordingly, Applicants respectfully submit that one of skill in the art could reasonably conclude that Applicants had possession of the claimed invention, as described in amended claims 1 and 5, at the time the instant application was filed.

---

[4] See the paragraph carried over from page 3 to page 4, of the Office Action.
[5] See page 4, lines 1-2, of the Office Action.

Applicants further submit that new claims 24 and 28 directed to a polynucleotide that 1) hybridizes to a polynucleotide that encodes the polypeptide of SEQ ID NO:4 and 2) encodes for a polypeptide having alpha galactosidase activity also fulfill the written description requirement for patentability under 35 U.S.C. § 112, first paragraph.

New claims 29 and 30 are directed to a fragment comprising a nucleic acid sequence of a portion of the polynucleotides of the claimed invention and, wherein, the fragment encodes a polypeptide having alpha galactosidase activity. Thus, Applicants have sufficiently described the claimed polynucleotide in terms of its structure and function as to meet the requirements for patentability under 35 U.S.C. § 112, first paragraph.

New claims 31-41 are directed to a fragment consisting of a sequence of a portion of the claimed invention and polynucleotides and, wherein, the fragment is capable of identifying a polypeptide having alpha galactosidase activity. Some exemplary uses of these fragments are as probes or primers for detection, nucleotide capture, or screening methods. Thus, Applicants have sufficiently described the claimed polynucleotide in terms of its structure and function as to meet the requirements for patentability under 35 U.S.C. § 112, first paragraph.

New claims 42-45 are directed to a polynucleotide probe comprising the fragments of the claimed invention. Thus, Applicants have sufficiently described the claimed polynucleotide in terms of its structure and function as to meet the requirements for patentability under 35 U.S.C. § 112, first paragraph.

The Patent Office alleges that claim 19 claims a genus of polynucleotides that encode polypeptides with or without any enzymatic activity, and, as such, fails to sufficiently describe the claimed genus of polynucleotides.[6] Applicants have amended claim 19 to more particularly describe the invention. Applicants submit, however, that claim 19 incorporates the limitations of claims 1, 13, and 14, wherein all the claimed polynucleotides encode for a polypeptide having alpha galactosidase activity. Thus, the amendment to claim 19 does not change the scope of claim 19.

---

[6] See, page 4, lines 20-23, of the Office Action.

Enablement

Claims 1-3, 5-9, and 17-23 are rejected under 35 U.S.C. §112, first paragraph, because it is alleged that the specification, while being enabling for the polynucleotide of SEQ ID NO:3, does not reasonably provide enablement for all polynucleotides having at least 70% or 90% identity to a polynucleotide encoding an alpha galactosidase comprising SEQ ID NO:4 (part (a) of claims 1 and 5, respectively), all polynucleotides comprising at least 30 nucleotides thereof (part (c) of claims 1 and 5). The Patent Office alleges that claims 1, 5, 13, 14, and claims depending therefrom, are so broad as to encompass all polynucleotides comprising homologues or fragments of a polynucleotide encoding SEQ ID NO:4 as encompassed by the claims. Thus, the Patent Office concludes that the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. The Patent Office further concludes that applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims.[7]

Applicants respectfully disagree. In the present application, Applicants have disclosed the amino acid sequence (*i.e.,* structure) of a novel polypeptide having alpha galactosidase activity. It should be mentioned that, at the time the instant application was filed, the state of the art and level of skill of the artisan in the field of molecular biology was very advanced. Thus, armed with the disclosure provided in the application, one of ordinary skill in the art could use well-known laboratory techniques such as library screening and, with modifications based on the teachings of the instant application such as using the nucleic acid structure provided to create degenerate probes/primers, probe custom-made or commercially available libraries for polynucleotides that hybridize to the probes (or is amplified by the primers). These polynucleotides can be expressed by known methods to obtain polypeptides. The polypeptides can then be tested to see if they meet the requirements to be one of the claimed polynucleotides, *i.e.,* the nucleic acid is least 70% identical to a polynucleotide that encodes a polypeptide (*e.g.,* SEQ ID NO:4) having alpha galactosidase activity. The application provides ample teaching of

[7] See, page 4, to page 6, of the Office Action.

how to test for measuring percent identity/similarity on page 6, lines 12-21 and how to test for alpha galactosidase activity on pages 22-23 in the section entitled "Screening for glycosidase activity." It would be a matter of routine experimentation, not undue experimentation, for one skilled in the art to find polynucleotides having at least 70% identical to SEQ ID NO:4, or those that would hybridize to SEQ ID NO:4, and having galactosidase activity.

Regarding undue experimentation, as stated by the Patent Office, the Federal Circuit in *In re Wands* directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" is set forth by the Federal Circuit in, *e.g.*, *Hybritech, Inc. v. Monoclonal Antibodies, Inc.* In that case, an applicant had claims that were generic to all IgM antibodies directed to a specific antigen. However, only a single antibody producing cell line had been deposited. The PTO had rejected claims that were generic to all antibodies directed to the antigen as lacking an enabling disclosure.

The Federal Circuit reversed, noting that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody species was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of molecular biology for the instant invention also recognize that many rounds of screening may be necessary to isolate the claimed polynucleotides. The procedures for isolating polynucleotides are widely accepted, routine protocols, not requiring

"undue experimentation" to be practiced. Accordingly, one skilled in the art is provided sufficient guidance by the specification to practice the claimed methods without undue experimentation.

While the disclosure does not provide the sequences of all the polynucleotides of the invention, the specification does provide guidance for one of skill in the art on how to obtain/create the polynucleotides of the invention. Applicants submit that techniques such as the use of probes or primers to screen libraries are standard research techniques for isolating polynucleotides and polypeptides for which they encode. Other methods are also known in the art. Applicants further submit that, while the practice will generate leads that will eventually be found not to be one of the claimed polynucleotides, this alone does not make such techniques non-enabling. Applicants have provided exemplary methods for obtaining polynucleotides of the invention, as well as methods for recognizing which polynucleotides are those of the claimed invention, *i.e.*, the structure of the claimed polynucleotides of the invention (*e.g.*, at least 70% identity to SEQ ID NO:4 or that hybridize to SEQ ID NO:4) and an assay to test the function of the polypeptides encoded by the polynucleotides of the claimed invention. Applicants respectfully submit that the skilled artisan is provided with sufficient disclosure to practice the full scope of the claimed invention.

The level of skill and knowledge in the art is exemplified by patents, which were filed before the filing date of the instant application, claiming a nucleic acid sequence or construct comprising a nucleotide sequence having at least 70% or more sequence identity. For example, in U.S. Patent No. 6,410,264, claim 1 reads:

> 1. A recombinant construct comprising in proper reading frame a nucleotide sequence for a promoter and a nucleotide sequence encoding a polypeptide, where said promoter drives transcription of an operably linked nucleotide sequence of interest, wherein said nucleotide sequence for said promoter is selected from the group consisting of:
>
> a) the nucleotide sequence set forth in SEQ ID NO: 2;
>
> b) a nucleotide sequence having at least 70% sequence identity to the

nucleotide sequence set forth in SEQ ID NO: 2;

c) a nucleotide sequence comprising at least 24 contiguous nucleotides of the sequence set forth in SEQ ID NO: 2; and

d) a nucleotide sequence that hybridizes to any one of a), b), or c) under conditions of high stringency.

Applicants have attached other issued claims reciting the claimed composition in terms of percent homology to a particular SEQ ID NO. Applicants respectfully submit that the application, at the time of filing, taught one of skill in the art how to make and use the claimed invention.

In light of the foregoing reasons, Applicants respectfully submit that the specification provides sufficient written description and provides sufficient written description to fully enable the skilled artisan to practice the full scope of the invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-3, 5-9, and 17-23 under 35 U.S.C. §112, first paragraph.

Previously raised issue under 35 U.S.C. §102

In a previous Office Action mailed August 31, 2000, the Patent Office cited U.S. Patent No. 5,686,294 to Sogabe *et al.* (hereinafter "Sogabe") against the claims of the instant application. The Patent Office cited Sogabe for allegedly teaching at least 15 nucleotides of SEQ ID NO:4, as well as vectors comprising the polynucleotide, transformed host cells, and a method of making proteins.[8]

Sogabe teaches a protein having heat-resistant malate dehydrogenase activity and a DNA fragment having a gene encoding said protein. In contrast, Applicants claimed invention is drawn to proteins having alpha galactosidase activity. Fragments of Applicants' claimed invention either encode polypeptides having alpha galactosidase activity or are capable of identifying a polynucleotide encoding a polypeptide having alpha galactosidase activity.

[8] See page 6, item 17, carried over to page 7, of the Office Action mailed August 31, 2001.

Sogabe does not teach a protein having alpha galactosidase activity or a fragment having alpha galactosidase activity. Nor does Sogabe teach a nucleic acid fragment, by itself or as a probe, capable of identifying a polynucleotide encoding a polypeptide having alpha galactosidase activity. Sogabe does not even contemplate the property of alpha galactosidase activity in its invention. Because Sogabe does not teach each and every element of the claimed invention, it does not anticipate Applicants' claimed invention.

CONCLUSION

Claims 1-9, 13, 14, and 17-23 are pending in the application. Claims 1, 5, 9, 13, 14, and 19 have been amended; and claims 24-45 have been added by the instant Response. Applicants request that the Examiner reconsider the application and claims in light of the foregoing reasons and amendments and respectfully submit that the claims are in condition for allowance.

If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity to discuss any outstanding issues and to work with the Examiner toward placing the application in condition for allowance.

Attached is a marked-up version of the changes being made by the current amendment.

Applicants believe that no fees are necessitated by the present Response. However, in the event any fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

Respectfully submitted,

Date: August 9, 2002

Mi K. Kim
Reg. No. 44,830

Fish & Richardson P.C.
PTO Customer No. 20985
4350 La Jolla Village Drive, Suite 500
San Diego, California 92122
Telephone: (858) 678-5070
Facsimile: (858) 678-5099

Version with markings to show changes made

In the specification:

The title on page 1 has been amended as follows:

ALPHA-GALACTOSIDASE ENZYMES, NUCLEIC ACIDS ENCODING THEM AND METHODS OF MAKING AND USING THEM

In the claims:

Claims 1, 5, 9, 13, 14, and 19 have been amended as follows:

1. (Thrice Amended) An isolated polynucleotide comprising a member selected from the group consisting of:

(a) a polynucleotide having at least a 70% identity to a polynucleotide encoding an enzyme comprising the amino acid sequence set forth in SEQ ID NO: 4 and having alpha galactosidase activity; and

(b) a polynucleotide that is complementary to a polynucleotide of (a).[; and

(c) a polynucleotide comprising at least 30 bases of a polynucleotide of (a) or (b).]

5. (Twice Amended) An isolated polynucleotide comprising a member selected from the group consisting of:

(a) a polynucleotide having at least a 90% identity to a polynucleotide encoding an enzyme having a sequence as set forth in SEQ ID NO:4 and having alpha galactosidase activity; and

(b) a polynucleotide complementary to a polynucleotide of (a).[; and

(c) a polynucleotide comprising at least 30 bases of a polynucleotide of (a) and (b).]

9. (Amended) A process for producing a cell that expresses the polypeptide encoded by a DNA contained in a vector comprising transforming or transfecting the cell with the vector of claim [Claim] 6 [such that the cell expresses the polypeptide encoded by the DNA contained in the vector].

13. (Twice Amended) The polynucleotide of claim 1, wherein the polynucleotide has at least 95% [70%] identity to a polynucleotide encoding [an enzyme comprising] the amino acid sequence set forth in SEQ ID NO:4 and encodes a protein having alpha galactosidase activity.

14. (Thrice Amended) The polynucleotide of claim 13, wherein the polynucleotide has at least 97% [90%] identity to a polynucleotide encoding an alpha galactosidase comprising the amino acid sequence set forth in SEQ ID NO:4.

19. (Thrice Amended) The polynucleotide of claim 18, wherein the single stranded DNA is a coding sequence of a polypeptide having alpha galactosidase activity.